June 7, 1957

Dr. Bill Hayes
London Postgraduate Medical School
London, England

Dear Bill:

At the Ciba meetings, I had not taken my own qualifications about the dominance of Az^r as more than a scholastic exercise, but now I am beginning to wonder whether they may have to be looked at more seriously. Since coming back we've resuscitated the Az^r/Az^s diploids, and as far as we can judge, the Az^r character is recessive. That is to say, on EMB lactose agar plus M/500 azide, the heterozygous cells fail to give colonies. The same diploid stock is throwing haploid segregants, some also sensitive, some resistant to this level of azide.

We've had no thought of going into this problem very seriously -- I only got Miss Cook here to look into it in hopes of rounding out your own very nice story with an independent confirmation. But now we have the problem of reconciling the two sets of facts. It seems to me improbable that the two tests, in principle, should give different answers; if anything, the peristent diploids ought to show the action of the Az^r gene more strongly than the newly formed ones. So it would appear that either the difference in stocks, or the conditions of test, are behind it.

As to the former, I have no convenient way of getting your Az^r into a diploid; it could be done, but the stock-building would be rather elaborate, and the more difficult as I have very little experience with Hfr_h. The Az^r we're using is in an F^+ Het M^- stock -- in fact of the various Het stocks stored away, it seems to be the most like the original in giving fair yields of diploid progeny. Do you think you could manage a comparable analysis of phenotypic expression with an F^+ parent? Alternatively, I am anxious anyhow to have an Hfr Het, and am screening for an Hfr mutant, and if successful this would furnish better material. Needless to say, if you intend to give this matter your continued close attention, I will be happy to furnish any of the materials mentioned, as well as a representative Az^r/Az^s diploid.

The second question is the screening method. I am a little concerned about the low concentration (M/1600) of azide that you use for your platings in minimal agar. The JGM paper does not amplify how it was determined that M/1600 was optimally differential. Is that just too obvious, that you compared Az^r and Az^s prototrophs? I am also a bit puzzled about your remarks on M/500 in nutrient agar. (p.106). Are you just quoting me, or do you concur, and is this a differential concentration for your stocks also?

We have in the works a final trial, to see how the heterozygote grows on your minimal agar—perhaps this will give a direct answer to some of these questions. P.S. Is .1% sodium aspartate as aspartic acid or the salt? Will asparagine do as well?

Sincerely,

Joshua Lederberg